

CLAIMS:

1. A composition comprising:

- (a) a virus-like particle;
- (b) at least one immunostimulatory substance; and
- (c) at least one antigen or antigenic determinant;

wherein said at least one antigen or antigenic determinant is bound to said virus-like particle, and wherein said immunostimulatory substance is bound to said virus-like particle, and wherein said antigen comprises, alternatively consists essentially of, or alternatively consists of at least one HIV polypeptide.

2. The composition of claim 1, wherein said at least one antigen or antigenic determinant is bound to said virus-like particle by at least one covalent bond, and wherein preferably said covalent bond is a non-peptide bond.

3. The composition of claim 1, wherein said at least one antigen or antigenic determinant is fused to said virus-like particle.

4. The composition of any of the preceding claims, wherein said at least one HIV polypeptide is selected from:

- (a) HIV protein subunit p17-GAG;
- (b) HIV protein subunit p24-GAG;
- (c) HIV protein subunit p15-GAG;
- (d) HIV protein subunit Protease;
- (e) HIV protein subunit reverse transcriptase (RT);
- (f) HIV protein subunit Integrase;
- (g) HIV protein subunit Vif;
- (h) HIV protein subunit Vpr;
- (i) HIV protein subunit Vpu;
- (j) HIV protein subunit Tat;
- (k) HIV protein subunit Rev
- (l) HIV protein subunit gp-41-Env;
- (m) HIV protein subunit gp-120-Env;

- (n) HIV protein subunit Nef;
(o) Nef-protein consensus sequence (SEQ ID NO: 75);
(p) GAG consensus sequence (SEQ ID NO: 76); and
(q) any fragment of any of the HIV protein subunits or consensus
sequences from (a) to (p).

5. The composition of any of the preceding claims, wherein said at least one HIV polypeptide is selected from:

- (a) HIV protein subunit p24-GAG;
(b) HIV protein subunit Nef;
(c) Nef-protein consensus sequence (SEQ ID NO: 75);
(d) GAG consensus sequence (SEQ ID NO: 76);
(e) any fragment of any of the HIV protein subunits or consensus
sequences from (a) to (d).

6. The composition of any of the preceding claims, wherein said at least one HIV polypeptide has the amino acid sequence of Nef-protein consensus sequence (SEQ ID NO: 75), GAG consensus sequence (SEQ ID NO: 76), or a fragment thereof.

7. The composition of any of the preceding claims, wherein said at least one HIV polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 77;
(b) the amino acid sequence of SEQ ID NO: 78;
(c) the amino acid sequence of SEQ ID NO: 80;
(d) the amino acid sequence of SEQ ID NO: 81;
(e) the amino acid sequence of SEQ ID NO: 82;
(f) the amino acid sequence (SEQ ID NO: 100);
(g) the amino acid sequence (SEQ ID NO: 102),
(h) the amino acid sequence (SEQ ID NO: 114);
(i) the amino acid sequence (SEQ ID NO: 116); and
(j) any fragment of any of the sequences from (a) to (i).

8. The composition of any of the preceding claims, wherein said antigen is a combination of at least two HIV polypeptides, wherein said at least two HIV polypeptides are bound directly or by way of a linking sequence.
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9. The composition of claim 8, wherein each of said at least two HIV polypeptides are selected from
- (a) HIV protein subunit p24-GAG;
 - (b) HIV protein subunit Nef;
 - 10 (c) Nef-protein consensus sequence (SEQ ID NO: 75);
 - (d) GAG consensus sequence (SEQ ID NO: 76);
 - (e) any fragment of any of the HIV protein subunits or consensus sequences from (a) to (d).
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10. The composition of claim 8, wherein said at least two HIV polypeptides are a combination of at least one HIV polypeptide selected from Nef-protein consensus sequence (SEQ ID NO: 75) or a fragment thereof, and of at least one HIV polypeptide selected from GAG-protein consensus sequence (SEQ ID NO: 76) or a fragment thereof.
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11. The composition of claim 8, wherein said at least two HIV polypeptides comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:
- (a) the amino acid sequence of SEQ ID NO: 83;
 - 25 (b) the amino acid sequence of SEQ ID NO: 84;
 - (c) the amino acid sequence of SEQ ID NO: 86;
 - (d) any fragment of any of the sequences from (a) to (c).
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12. The composition of any of the preceding claims, wherein said virus-like particle comprises at least one first attachment site and wherein said antigen or antigenic determinant further comprises at least one second attachment site being selected from the group consisting of:

- (a) an attachment site not naturally occurring with said antigen or antigenic determinant; and
- (b) an attachment site naturally occurring with said antigen or antigenic determinant;

5 and wherein said binding of said antigen or antigenic determinant to said virus-like particle is effected through association between said first attachment site and said second attachment site, wherein preferably said association is through at least one non-peptide bond.

10 13. The composition of claim 12, wherein said antigen or antigenic determinant and said virus-like particle interact through said association to form an ordered and repetitive antigen array.

15 14. The composition of claim 12 or 13, wherein said first attachment site comprises, or preferably consists of, an amino group or a lysine residue.

20 15. The composition of any of the claims 12 to 14, wherein said second attachment site comprises, or preferably consists of, a sulfhydryl group or a cysteine residue.

 16. The composition of any of the claims 12 to 15, wherein said first attachment site is a lysine residue and said second attachment site is a cysteine residue.

25 17. The composition of any of the claims 12 to 16, wherein said first attachment site is an amino group and said second attachment site is a sulfhydryl group

30 18. The composition of any of the claims 12 to 17, wherein said said at least two HIV polypeptides with said second attachment site comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 72;
- (b) the amino acid sequence of SEQ ID NO: 85;
- (c) the amino acid sequence of SEQ ID NO: 87; and

- (d) any fragment of any of the sequences from (a) to (c).

19. The composition of claim any one of claim 1 to 3, wherein said antigen or antigenic determinant comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 71; and
(b) the amino acid sequence of SEQ ID NO: 73.

20. The composition of claim any one of the preceding claims, wherein said virus-like particle lacks a lipoprotein-containing envelope.

21. The composition of any one of the preceding claims, wherein said virus-like particle is a recombinant virus-like particle, wherein preferably said virus like particle is selected from the group consisting of:

- (a) recombinant proteins of Hepatitis B virus;
(b) recombinant proteins of measles virus;
(c) recombinant proteins of Sindbis virus;
(d) recombinant proteins of Rotavirus;
(e) recombinant proteins of Foot-and-Mouth-Disease virus;
(f) recombinant proteins of Retrovirus;
(g) recombinant proteins of Norwalk virus;
(h) recombinant proteins of human Papilloma virus;
(i) recombinant proteins of BK virus;
(j) recombinant proteins of bacteriophages;
(k) recombinant proteins of RNA-phages;
(l) recombinant proteins of Ty; and
(m) fragments of any of the recombinant proteins from (a) to (l).

22. The composition of any of the preceding claims, wherein said virus-like particle is the Hepatitis B virus core protein or the BK virus VP1 protein.

23. The composition of claim 22, wherein said HIV polypeptide is fused to the C-terminus of said Hepatitis B virus core protein or said BK virus VP1 protein, preferably, by way of a linking sequence.

5 24. The composition of any of the preceding claims, wherein said virus-like particle comprises, or alternatively consists essentially of, or alternatively consists of recombinant proteins, or fragments thereof, of a RNA-phage, wherein preferably said RNA-phage is selected from the group consisting of:

- 10 (a) bacteriophage Q β ;
- (b) bacteriophage R17;
- (c) bacteriophage fr;
- (d) bacteriophage GA;
- (e) bacteriophage SP;
- (f) bacteriophage MS2;
- 15 (g) bacteriophage M11;
- (h) bacteriophage MX1;
- (i) bacteriophage NL95;
- (j) bacteriophage f2;
- (k) bacteriophage PP7; and
- 20 (l) bacteriophage AP205.

25 25. The composition of any one of the preceding claims, wherein said virus-like particle comprises, or alternatively consists essentially of, or alternatively consists of recombinant proteins, or fragments thereof, of bacteriophage Q β or bacteriophage AP205.

30 26. The composition of any one of the preceding claims, wherein said immunostimulatory substance is a toll-like receptor activating substance or cytokine secretion inducing substance, wherein preferably said toll-like receptor activating substance is selected from the group consisting of, or alternatively consists essentially of:

- (a) immunostimulatory nucleic acids;
- (b) peptidoglycans;

- (c) lipopolysaccharides;
(d) lipoteichonic acids;
(e) imidazoquinoline compounds;
(f) flagellines;
(g) lipoproteins;
(h) immunostimulatory organic molecules;
(i) unmethylated CpG-containing oligonucleotides; and
(j) any mixtures of at least one substance of (a), (b), (c), (d), (e), (f), (g), (h) and/or (i).

27. The composition of claim 26, wherein said immunostimulatory nucleic acid is selected from the group consisting of, or alternatively consists essentially of:

- (a) ribonucleic acids;
(b) deoxyribonucleic acids;
(c) chimeric nucleic acids; and
(d) any mixtures of at least one nucleic acid of (a), (b) and/or (c).

28. The composition of claim 27, wherein said ribonucleic acid is poly-(I:C) or a derivative thereof.

29. The composition of claim 27, wherein said deoxyribonucleic acid is selected from the group consisting of, or alternatively consists essentially of:

- (a) unmethylated CpG-containing oligonucleotides; and
(b) oligonucleotides free of unmethylated CpG motifs.

30. The composition of any one of claim 1 to 27 and claims 29, wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide.

31. The composition of claim 30, wherein said unmethylated CpG-containing oligonucleotide comprises the sequence:

5' X1X2CGX3X4 3'

wherein X1, X2, X3, and X4 are any nucleotide.

32. The composition of claim 31, wherein at least one of said nucleotide X1, X2, X3, and X4 has a phosphate backbone modification.

5 33. The composition of any one of the preceding claims, wherein said at least one immunostimulatory substance, and preferably said unmethylated CpG-containing oligonucleotide, comprises, or alternatively consists essentially of, or alternatively consists of a palindromic sequence.

10 34. The composition of claim 30, wherein said unmethylated CpG-containing oligonucleotide comprises, or alternatively consists essentially of, or alternatively consists of the sequence selected from the group consisting of:

(a) TCCATGACGTTCTGAATAAT (SEQ ID NO: 35);

(b) TCCATGACGTTCTGACGTT (SEQ ID NO: 37);

15 (c) GGGGTCAACGTTGAGGGG (SEQ ID NO: 39);

(d) GGGGGGGGGGACGATCGTCGGGGGGGGG (SEQ ID NO: 41); and

(e) "dsCyCpG-253" (SEQ ID NO: 49) as described in Table 2,

20 and wherein preferably said unmethylated CpG-containing oligonucleotide contains one or more phosphorothioate modifications of the phosphate backbone or wherein each phosphate moiety of said phosphate backbone of said oligonucleotide is a phosphorothioate modification.

25 35. The composition of claim 30, wherein said unmethylated CpG-containing oligonucleotide comprises, or alternatively consists essentially of, or alternatively consists of the sequence
GGGGGGGGGGACGATCGTCGGGGGGGGG (SEQ ID NO: 41).

30 36. The composition of claim 28, wherein said palindromic unmethylated CpG-containing oligonucleotide contains one or more phosphorothioate modifications of the phosphate backbone or wherein each phosphate moiety of said phosphate backbone of said oligonucleotide is a phosphorothioate modification.

37. The composition of any of the preceding claims, wherein said at least one immunostimulatory substance, and preferably said immunostimulatory nucleic acid, and even more preferably said unmethylated CpG-containing
5 oligonucleotide contains one or more phosphorothioate modifications of the phosphate backbone or wherein each phosphate moiety of said phosphate backbone of said oligonucleotide is a phosphorothioate modification.
38. The composition of any one of the preceding claims, wherein said
10 immunostimulatory substance is non-covalently bound to said virus-like particle.
39. The composition of any one of the preceding claims, wherein said at least one immunostimulatory substance, and preferably said unmethylated CpG-containing oligonucleotide is non-covalently bound to said virus-like particle.
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40. The composition of any of the preceding claims, wherein said at least one immunostimulatory substance, and preferably said immunostimulatory nucleic acid, and even more preferably said unmethylated CpG-containing
20 oligonucleotide, comprises about 6 to about 100,000 nucleotides, preferably about 6 to about 2000 nucleotides, and more preferably about 20 to about 500 nucleotides, and even more preferably about 20 to about 100 nucleotides.
41. The composition of any of the preceding claims, wherein said at least one immunostimulatory substance, and preferably said immunostimulatory nucleic
25 acid, and even more preferably said unmethylated CpG-containing oligonucleotide, is selected from
- (a) a recombinant oligonucleotide;
 - (b) a genomic oligonucleotide;
 - (c) a synthetic oligonucleotide;
 - 30 (d) a plasmid-derived oligonucleotide;
 - (e) a single-stranded oligonucleotide; and
 - (f) a double-stranded oligonucleotide.

42. The composition of claim 30, wherein said palindromic sequence comprises, or alternatively consists essentially of, or alternatively consists of GACGATCGTC (SEQ ID NO: 1).
- 5 43. The composition of claim 42, wherein said palindromic sequence is flanked at its 5'-terminus by at least 3 and at most 10 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus by at least 6 and at most 10 guanosine entities.
- 10 44. The composition of claim 42, wherein said palindromic sequence is flanked at its 5'-terminus of at least 4 and at most 10 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus of at least 6 and at most 10 guanosine entities.
- 15 45. The composition of claim 42, wherein said palindromic sequence is flanked at its 5'-terminus of at least 5 and at most 10 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus of at least 6 and at most 10 guanosine entities.
- 20 46. The composition of claim 42, wherein said unmethylated CpG-containing oligonucleotide has a nucleic acid sequence selected from
- (a) GGGGACGATCGTCGGGGG ((SEQ ID NO: 2);
 - (b) GGGGGACGATCGTCGGGGG ((SEQ ID NO: 3);
 - (c) GGGGGGACGATCGTCGGGGG ((SEQ ID NO: 4);
 - 25 (d) GGGGGGGACGATCGTCGGGGG ((SEQ ID NO: 5);
 - (e) GGGGGGGGACGATCGTCGGGGG ((SEQ ID NO: 6);
 - (f) GGGGGGGGACGATCGTCGGGGGG ((SEQ ID NO: 7);
 - (g) GGGGGGGGGACGATCGTCGGGGGGG ((SEQ ID NO: 8);
 - (h) GGGGGGCGACGACGATCGTCGTCGGGGGG ((SEQ ID NO: 9);
 - 30 and
 - (i) GGGGGGGGGGACGATCGTCGGGGGGGGG (SEQ ID NO: 41).

47. The composition of claim 30 or 42, wherein said unmethylated CpG-containing oligonucleotide has a nucleic acid sequence of SEQ ID NO: 7 or SEQ ID NO: 41.

5 48. The composition of any one of the preceding claims, wherein said antigen comprises a cytotoxic T cell epitope, a Th cell epitope or a combination of at least two of said epitopes, wherein said at least two epitopes are bound directly or by way of a linking sequence, and wherein preferably said cytotoxic T cell epitope is a viral or a tumor cytotoxic T cell epitope.

10 49. A method for enhancing an immune response in an animal comprising introducing into said animal a composition comprising:

- (a) a virus-like particle;
- (b) at least one immunostimulatory substance; and
- 15 (c) at least one antigen or antigenic determinant;

wherein said at least one antigen or antigenic determinant is bound to said virus-like particle, and wherein said immunostimulatory substance is bound to said virus-like particle, and wherein said antigen comprises, alternatively consists essentially of, or alternatively consists of at least one HIV polypeptide.

20 50. The method of claim 49, wherein said at least one antigen or antigenic determinant is bound to said virus-like particle by at least one covalent bond, and wherein said covalent bond is a non-peptide bond.

25 51. The method of claim 49, wherein said at least one antigen or antigenic determinant is fused to said virus-like particle.

52. The method of any one of claim 49 to 51, wherein said at least one HIV polypeptide is selected from:

- 30 (a) HIV protein subunit p17-GAG;
- (b) HIV protein subunit p24-GAG;
- (c) HIV protein subunit p15-GAG;
- (d) HIV protein subunit Protease;

- (e) HIV protein subunit reverse transcriptase (RT);
(f) HIV protein subunit Integrase;
(g) HIV protein subunit Vif;
(h) HIV protein subunit Vpr;
5 (i) HIV protein subunit Vpu;
(j) HIV protein subunit Tat;
(k) HIV protein subunit Rev
(l) HIV protein subunit gp-41-Env;
(m) HIV protein subunit gp-120-Env;
10 (n) HIV protein subunit Nef;
(o) Nef-protein consensus sequence (SEQ ID NO: 75);
(p) GAG consensus sequence (SEQ ID NO: 76); and
(q) any fragment of any of the HIV protein subunits or consensus
sequences from (a) to (p).

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53. The method of any one of claim 49 to 51, wherein said at least one HIV polypeptide is selected from:

- (a) HIV protein subunit p24-GAG;
(b) HIV protein subunit Nef;
20 (c) Nef-protein consensus sequence (SEQ ID NO: 75);
(d) GAG consensus sequence (SEQ ID NO: 76);
(e) any fragment of any of the HIV protein subunits or consensus
sequences from (a) to (d).

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54. The method of any one of claim 49 to 51, wherein said at least one HIV polypeptide has the amino acid sequence of Nef-protein consensus sequence (SEQ ID NO: 75), GAG consensus sequence (SEQ ID NO: 76), or a fragment thereof.

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55. The method of any one of claim 49 to 51, wherein said at least one HIV polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 77;

- (b) the amino acid sequence of SEQ ID NO: 78;
- (c) the amino acid sequence of SEQ ID NO: 80;
- (d) the amino acid sequence of SEQ ID NO: 81;
- (e) the amino acid sequence of SEQ ID NO: 82;
- 5 (f) the amino acid sequence (SEQ ID NO: 100);
- (g) the amino acid sequence (SEQ ID NO: 102),
- (h) the amino acid sequence (SEQ ID NO: 114);
- (i) the amino acid sequence (SEQ ID NO: 116); and
- 10 (j) any fragment of any of the sequences from (a) to (e).

56. The method of any one of claim 49 to 51, wherein said antigen is a combination of at least two HIV polypeptides, wherein said at least two HIV polypeptides are bound directly or by way of a linking sequence.

15 57. The method of claim 56, wherein each of said at least two HIV polypeptides are selected from

- (a) HIV protein subunit p24-GAG;
- (b) HIV protein subunit Nef;
- (c) Nef-protein consensus sequence (SEQ ID NO: 75);
- 20 (d) GAG consensus sequence (SEQ ID NO: 76);
- (e) any fragment of any of the HIV protein subunits or consensus sequences from (a) to (d).

25 58. The method of claim 56, wherein said at least two HIV polypeptides are a combination of at least one HIV polypeptide selected from Nef-protein consensus sequence (SEQ ID NO: 75) or a fragment thereof, and of at least one HIV polypeptide selected from GAG-protein consensus sequence (SEQ ID NO: 76) or a fragment thereof.

30 59. The method of claim 56, wherein said at least two HIV polypeptides comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 83;

- (b) the amino acid sequence of SEQ ID NO: 84;
- (c) the amino acid sequence of SEQ ID NO: 86;
- (d) any fragment of any of the sequences from (a) to (c).

- 5 60. The method of any one of claim 49 to 59, wherein said virus-like particle comprises at least one first attachment site and wherein said antigen or antigenic determinant further comprises at least one second attachment site being selected from the group consisting of:
- 10 (a) an attachment site not naturally occurring with said antigen or antigenic determinant; and
- (b) an attachment site naturally occurring with said antigen or antigenic determinant;
- and wherein said binding of said antigen or antigenic determinant to said virus-like particle is effected through association between said first attachment
- 15 site and said second attachment site, wherein preferably said association is through at least one non-peptide bond.
61. The method of claim 60 wherein said antigen or antigenic determinant and said virus-like particle interact through said association to form an ordered and
- 20 repetitive antigen array.
62. The method of claim 60 or 61, wherein said first attachment site comprises, or preferably consists of, an amino group or a lysine residue.
- 25 63. The method of any of the claims 60 to 62, wherein said second attachment site comprises, or preferably consists of, a sulfhydryl group or a cysteine residue.
64. The method of any of the claims 60 to 63, wherein said first attachment site is a lysine residue and said second attachment site is a cysteine residue.
- 30 65. The method of any of the claims 60 to 64, wherein said first attachment site is an amino group and said second attachment site is a sulfhydryl group.

66. The method of any of claims 60 to 65, wherein said said at least two HIV polypeptides with said second attachment site comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:
- (a) the amino acid sequence of SEQ ID NO: 72;
 - (b) the amino acid sequence of SEQ ID NO: 85;
 - (c) the amino acid sequence of SEQ ID NO: 87; and
 - (d) any fragment of any of the sequences from (a) to (c).
67. The method of any one of claim 49 to 51, wherein said antigen or antigenic determinant comprise, alternatively consist essentially of, or alternatively consist of an amino acid sequence selected from:
- (a) the amino acid sequence of SEQ ID NO: 71; and
 - (b) the amino acid sequence of SEQ ID NO: 73.
68. The method of any one of claim 49 to 67, wherein said virus-like particle is a recombinant virus-like particle, wherein preferably said virus-like particle is selected from the group consisting of:
- (a) recombinant proteins of Hepatitis B virus;
 - (b) recombinant proteins of measles virus;
 - (c) recombinant proteins of Sinbis virus;
 - (d) recombinant proteins of Rotavirus;
 - (e) recombinant proteins of Foot-and-Mouth-Disease virus;
 - (f) recombinant proteins of Retrovirus;
 - (g) recombinant proteins of Norwalk virus;
 - (h) recombinant proteins of human Papilloma virus;
 - (i) recombinant proteins of BK virus;
 - (j) recombinant proteins of bacteriophages;
 - (k) recombinant proteins of RNA-phages;
 - (l) recombinant proteins of Ty; and
 - (m) fragments of any of the recombinant proteins from (a) to (l).
69. The method of claim 68, wherein said virus-like particle is the Hepatitis B virus core protein or the BK virus VP1 protein.

70. The method of any one of claim 49 to 67, wherein said virus-like particle comprises recombinant proteins, or fragments thereof, of a RNA-phage, and wherein preferably said RNA-phage is selected from the group consisting of:

- 5 (a) bacteriophage Q β ;
- (b) bacteriophage R17;
- (c) bacteriophage fr;
- (d) bacteriophage GA;
- (e) bacteriophage SP;
- 10 (f) bacteriophage MS2;
- (g) bacteriophage M11;
- (h) bacteriophage MX1;
- (i) bacteriophage NL95;
- (j) bacteriophage f2;
- 15 (k) bacteriophage PP7; and
- (l) bacteriophage AP205.

71. The method of any of claims 49 to 70, wherein said virus-like particle comprises, or alternatively consists essentially of, or alternatively consists of recombinant proteins, or fragments thereof, of bacteriophage Q β or bacteriophage AP205.

72. The method of any one of claim 49 to 71, wherein said immunostimulatory substance is a toll-like receptor activating substance or a cytokine secretion inducing substance, and wherein preferably said toll-like receptor activating substance is selected from the group consisting of, or alternatively consists essentially of:

- (a) immunostimulatory nucleic acids;
- (b) peptidoglycans;
- 30 (c) lipopolysaccharides;
- (d) lipoteichonic acids;
- (e) imidazoquinoline compounds;
- (f) flagellines;

- (g) lipoproteins;
- (h) immunostimulatory organic molecules;
- (i) unmethylated CpG-containing oligonucleotides; and
- (j) any mixtures of at least one substance of (a), (b), (c), (d), (e), (f), (g),
(h) and/or (i).

73. The method of claim 72, wherein said immunostimulatory nucleic acid is selected from the group consisting of, or alternatively consists essentially of:

- (a) ribonucleic acids;
- (b) deoxyribonucleic acids;
- (c) chimeric nucleic acids; and
- (d) any mixtures of at least one nucleic acid of (a), (b) and/or (c).

74. The method of claim 73, wherein said ribonucleic acid is poly-(I:C) or a derivative thereof.

75. The method of claim 73, wherein said deoxyribonucleic acid is selected from the group consisting of, or alternatively consists essentially of:

- (a) unmethylated CpG-containing oligonucleotides; and
- (b) oligonucleotides free of unmethylated CpG motifs.

76. The method of any one of claim 49 to 73 and claim 75, wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide.

77. The method of claim 76, wherein said unmethylated CpG-containing oligonucleotide comprises the sequence:



wherein X_1 , X_2 , X_3 , and X_4 are any nucleotide.

78. The method of claim 77, wherein said at least one of said nucleotide X_1 , X_2 , X_3 , and X_4 has a phosphate backbone modification.

79. The method of any of claims 49 to 77, wherein said at least one immunostimulatory substance, and preferably said unmethylated CpG-containing oligonucleotide, comprises, or alternatively consists essentially of, or alternatively consists of a palindromic sequence.

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80. The method of claim 76, wherein said unmethylated CpG-containing oligonucleotide comprises, or alternatively consists essentially of, or alternatively consists of the sequence selected from the group consisting of:

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- (a) TCCATGACGTTCTGAATAAT (SEQ ID NO: 35);
- (b) TCCATGACGTTCTGACGTT (SEQ ID NO: 37);
- (c) GGGGTCAACGTTGAGGGGG (SEQ ID NO: 39);
- (d) GGGGGGGGGGACGATCGTCGGGGGGGGG (SEQ ID NO: 41); and
- (e) "dsCyCpG-253" (SEQ ID NO: 49) as described in Table 2;

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and wherein preferably said unmethylated CpG-containing oligonucleotide contains one or more phosphorothioate modifications of the phosphate backbone or wherein each phosphate moiety of said phosphate backbone of said oligonucleotide is a phosphorothioate modification.

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81. The method of claim 76, wherein said unmethylated CpG-containing oligonucleotide is palindromic, and wherein preferably said palindromic unmethylated CpG-containing oligonucleotide comprises, or alternatively consists essentially of, or alternatively consists of the sequence GGGGGGGGGGACGATCGTCGGGGGGGGG (SEQ ID NO: 41)

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82. The method of any of claims 49 to 81, wherein said at least one immunostimulatory substance, and preferably said immunostimulatory nucleic acid, and even more preferably said unmethylated CpG-containing oligonucleotide contains one or more phosphorothioate modifications of the phosphate backbone or wherein each phosphate moiety of said phosphate backbone of said oligonucleotide is a phosphorothioate modification.

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83. The method of any one of claim 49 to 82, wherein said immunostimulatory substance, and preferably said unmethylated CpG-containing oligonucleotide, is non-covalently bound to said virus-like particle.

5 84. The method of any one of claim 49 to 83, wherein said immunostimulatory substance, and preferably said unmethylated CpG-containing oligonucleotide, is packaged, preferably enclosed by said virus-like particle.

10 85. The method of any one of claim 49 to 84, wherein at least one immunostimulatory substance, and preferably said immunostimulatory nucleic acid, and even more preferably said unmethylated CpG-containing oligonucleotide, comprises about 6 to about 100,000 nucleotides, and preferably wherein said immunostimulatory nucleic acid, and preferably said unmethylated
15 CpG-containing oligonucleotide comprises 20 to 100 nucleotides.

86. The method of any one of claim 49 to 85, wherein said at least one immunostimulatory substance, and preferably said immunostimulatory nucleic acid, and even more preferably said unmethylated CpG-containing
20 oligonucleotide, is selected from

- (a) a recombinant oligonucleotide;
- (b) a genomic oligonucleotide;
- (c) a synthetic oligonucleotide;
- (d) a plasmid-derived oligonucleotide;
- 25 (e) a single-stranded oligonucleotide; and
- (f) a double-stranded oligonucleotide.

87. The method of claim 79, wherein said palindromic sequence comprises, or alternatively consists essentially of, or alternatively consists of GACGATCGTC
30 (SEQ ID NO: 1).

88. The method of claim 87, wherein said palindromic sequence is flanked at its 5'-terminus by at least 3 and at most 10 guanosine entities and wherein said

palindromic sequence is flanked at its 3'-terminus by at least 6 and at most 10 guanosine entities.

89. The method of claim 87, wherein said palindromic sequence is flanked at its 5'-terminus of at least 4 and at most 10 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus of at least 6 and at most 10 guanosine entities.

90. The method of claim 87, wherein said palindromic sequence is flanked at its 5'-terminus of at least 5 and at most 10 guanosine entities and wherein said palindromic sequence is flanked at its 3'-terminus of at least 6 and at most 10 guanosine entities.

91. The method of claim 87, wherein said unmethylated CpG-containing oligonucleotide has a nucleic acid sequence selected from

- (a) GGGGACGATCGTCGGGGGG ((SEQ ID NO: 2);
 - (b) GGGGGACGATCGTCGGGGGG ((SEQ ID NO: 3);
 - (c) GGGGGGACGATCGTCGGGGGG ((SEQ ID NO: 4);
 - (d) GGGGGGGACGATCGTCGGGGGG ((SEQ ID NO: 5);
 - (e) GGGGGGGGACGATCGTCGGGGGGG ((SEQ ID NO: 6);
 - (f) GGGGGGGGGACGATCGTCGGGGGGGG ((SEQ ID NO: 7);
 - (g) GGGGGGGGGGACGATCGTCGGGGGGGGG ((SEQ ID NO: 8);
 - (h) GGGGGGCGACGACGATCGTCGTCGGGGGGG ((SEQ ID NO: 9);
- and
- (i) GGGGGGGGGGGACGATCGTCGGGGGGGGGG (SEQ ID NO: 41).

92. The method of claim 76 or 87, wherein said unmethylated CpG-containing oligonucleotide has a nucleic acid sequence of SEQ ID NO: 7 or or SEQ ID NO: 41.

93. The method of any one of claims 49 to 92, wherein said antigen comprises a cytotoxic T cell epitope, a Th cell epitope or a combination of at least two of

said epitopes, wherein said at least two epitopes are linked directly or by way of a linking sequence, and wherein preferably said cytotoxic T cell epitope is a viral or a tumor cytotoxic T cell epitope.

- 5 94. The method of any one of claims 49 to 92, wherein said immune response is an enhanced B cell response or an enhanced T cell response, wherein preferably said T cell response is a CTL response or a Th cell response, and wherein even more preferably said Th cell response is a Th1 cell response.
- 10 95. The method of any one of claims 49 to 94, wherein said animal is a mammal, and wherein preferably said mammal is a human.
96. The method of any one of claims 49 to 95, wherein said composition is introduced into said animal subcutaneously, intramuscularly, intravenously,
15 intranasally or directly into the lymph node.
97. A vaccine comprising an immunologically effective amount of the composition of any one of claim 1 to 48 together with a pharmaceutically acceptable diluent, carrier or excipient, and wherein preferably said vaccine further comprises an
20 adjuvant.
98. A method of immunizing or treating an animal comprising administering to said animal an immunologically effective amount of the vaccine of claim 97.
- 25 99. The method of claim 98, wherein said animal is a mammal, and wherein preferably said mammal is a human.
100. A method of immunizing or treating an animal comprising priming a T cell response in said animal by administering an immunologically effective amount
30 of the vaccine of claim 97.
101. The method of claim 100, further comprising the step of boosting the immune response in said animal, wherein preferably said boosting is effected by

administering an immunologically effective amount of a vaccine of claim 97 or an immunologically effective amount of a heterologous vaccine, wherein even more preferably said heterologous vaccine is a DNA vaccine.

- 5 102. A method of immunizing or treating an animal comprising the steps of priming a T cell response in said animal, and boosting a T cell response in said animal, wherein said boosting is effected by administering an immunologically effective amount of the vaccine of claim 97.
- 10 103. The method of claim 102, wherein said priming is effected by administering an immunologically effective amount of a vaccine of claim 97 or an immunologically effective amount of a heterologous vaccine, and wherein even more preferably said heterologous vaccine is a DNA vaccine.
- 15 104. An isolated polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:
- (a) the amino acid sequence of SEQ ID NO: 77;
 - (b) the amino acid sequence of SEQ ID NO: 78;
 - (c) the amino acid sequence of SEQ ID NO: 80;
 - 20 (d) the amino acid sequence of SEQ ID NO: 81;
 - (e) the amino acid sequence of SEQ ID NO: 82; and
 - (f) an amino acid sequence having at least 90% sequence identity to any of the amino acid sequences of (a) – (e) and being capable of being presented in a MHC complex.
- 25 105. An isolated polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:
- (a) the amino acid sequence of SEQ ID NO: 83;
 - (b) the amino acid sequence of SEQ ID NO: 84;
 - 30 (c) the amino acid sequence of SEQ ID NO: 86; and
 - (d) an amino acid sequence having at least 90% sequence identity to any of the amino acid sequences of (a) – (c) and being capable of being presented in a MHC complex.

106. An isolated polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 72;
- (b) the amino acid sequence of SEQ ID NO: 85;
- (c) the amino acid sequence of SEQ ID NO: 87; and
- (d) an amino acid sequence having at least 90% sequence identity to any of the amino acid sequences of (a) – (c) and being capable of being presented in a MHC complex.

107. An isolated polypeptide comprises, alternatively consists essentially of, or alternatively consists of an amino acid sequence selected from:

- (a) the amino acid sequence of SEQ ID NO: 71; and
- (b) the amino acid sequence of SEQ ID NO: 73;
- (c) an amino acid sequence having at least 90% sequence identity to any of the amino acid sequences of (a) – (b) and being capable of being presented in a MHC complex.